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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/023,711 | 12/21/2001 | Akira Imaizumi | 217576US0 | 6895 |

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| EXAMINER | |
|---|---|
| FRONDA, CHRISTIAN L | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1652 | |

DATE MAILED: 12/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/023,711 | IMAIZUMI ET AL. | |
| | Examiner | Art Unit | |
| | Christian L. Fronda | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,6,7 and 10-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6,7 and 10-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. The finality of the previous Office Action dated 06/15/2005 has been withdrawn in view of new rejections and grounds of rejection stated below.

2. Claims 1, 6, 7, 10-12 are under consideration in this Office Action.

3. The rejection of claims 7 and 12 under 35 U.S.C. 112, second paragraph, as being indefinite has been withdrawn in view of applicants' amendment to the claims filed on 10/14/2005.

### *Claim Rejections - 35 U.S.C. § 112, 1st Paragraph*

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 6, 7, and 10-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants' arguments filed 10/14/2005, have been fully considered but they are not persuasive. Applicants' position is that applicants are not required to recite the nucleotide sequence of the *E.coli* rmf gene which is well-known in the art, the examiner has not read the claims in light of the specification and prior art regarding the *E.coli* rmf gene, and that two exemplary amino acids are sufficient to describe the claimed genus of methods for producing any L-amino acid. The Examiner respectfully disagrees for reasons of record as supplemented below.

In the evaluation of the claims for compliance with the written description requirement of 35 U.S.C. 112, of particular relevance is 66 FR 1099, Friday, January 5, 2001,which states:

> "*Eli Lilly* explains that a chemical compound's name does not necessarily convey a written description of the named chemical compound, particularly when a genus of

> compounds is claimed. *Eli Lilly,* 119 F.3d at 1568, 43 USPQ2d at 1405. The name, if it does no more than distinguish the claimed genus from all others by function, does not satisfy the written description requirement because "it does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. *Eli Lilly,* 119 F.3d at 1568, 43 USPQ2d at 1406. Thus *Eli Lilly* identified a set of circumstances in which the words of the claim did not, without more, adequately convey to others that applicants had possession of what they claimed." (see p. 1100, 1st column, line 47 to 2nd column, line 2).

The claims are directed toward a genus of methods comprising culturing an *Escherichia coli* bacterium having a genus of rmf genes which encode RMF proteins that are inactive. The genus of rmf genes includes all allelic variants and mutants thereof, where the nature of such allelic variants is that they have differing structures and functions. Thus, the scope of this genus includes many members with widely differing structural, chemical, and physical properties. Furthermore, the genus is highly variable because a significant number of structural differences between genus members exists.

While the specification discloses the Yamagishi et al. reference and that a person of skill in the art would be expected to inactivate the rmf gene using methods well-known methods; the recitation of "*Escherichia coli* gene encoding the RMF protein" does not define any structural features and nucleotide sequences commonly possessed by the genus of rmf genes. Furthermore, the specification does not describe and define any structural features and nucleotide sequences commonly possessed by the genus. Thus, one skilled in the art cannot visualize or recognize the identity of the members of each genus for use in the claimed method.

Thus, one of skill in the art would not recognize that applicants were in possession of a genus of rmf genes that are mutated so that the RMF protein is inactive..

As stated in the previous Office Action the declaration under 37 CFR 1.132 filed 03/28/2005 is insufficient to overcome the rejection of the claims because the rmf gene disrupted strain only produced one other acidic amino acid which is glutamic acid. The specification only shows production of the basic amino acid lysine. However, the specification and the declaration under 37 CFR 1.132 filed 03/28/2005 do not describe production of any aliphatic amino acid (e.g., alanine), any aromatic amino acid (e.g., phenylalanine), any hydroxylic amino acid (e.g., serine), any sulphur-containing amino acid (e.g., cysteine), and any amide group containing amino acid (e.g., asparagines). The general knowledge of those skilled in the art do not provide

evidence that any other L-amino acid can be produced using the claimed method. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. In view of these considerations, one of skill in the art would conclude that Applicants have failed to sufficiently describe the claimed genus of methods, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed genus of methods for making any L-amino acid.

The claims are additionally rejected for the following reasons. Gene elements which are not particularly described, including regulatory elements, expression control sequences, and untranslated regions are essential to the function of the claimed invention since the claims recite a gene encoding the RMF protein . The art indicates that the structure of genes is empirically determined. For example, the structural elements of "gene" mediating the expression of a particular protein in the liver may be different than the structural elements of the "gene" mediating the expression of the same protein in the brain. Therefore, the structure of these elements which applicants considers as being essential to the function of the claim are not conventional in the art.

There is no known or disclosed correlation between the coding region of a polynucleotide encoding the RMF protein and the structure of the non-described regulatory elements, expression control sequences, and untranslated regions of the gene.

In view of the above considerations, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize applicants were in possession of any rmf gene.

6. Claims 7 and 12 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants' arguments filed 10/14/2005, have been fully considered but they are not persuasive. Applicants' positions is that the parent strain WC196 has been deposited under the Budapest Treaty and that plasmids used in the disruption of the rmf gene can be prepared from known plasmids pMAN031 and pUC19. The Examiner respectfully disagrees for reasons of record as supplemented below.

It is apparent that strain WC196Δrmf are required to practice the claimed invention. As such it must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the requirements of 35 USC § 112, first paragraph, may be satisfied by an enabling deposit of WC196Δrmf.

The process disclosed in the specification to make the strain WC196Δrmf does not appear to be repeatable. Example 2 of the specification discloses that crossover PCR was employed to disrupt the *E.coli* rmf gene, where primers of SEQ ID NOs: 1-4 were used. However, the specification does not disclose the specific nucleotide sequence of the inactivate rmf gene obtained by crossover PCR nor the specific portion of this inactivated rmf gene that was transformed and integrated into chromosome of the *E.coli* host cell.

Applicants' referral to deposit numbers for the parent strain is noted WC196 but is considered insufficient assurance that all of the conditions of 37 CFR 1.801-1.809 have been met since there the specification does not disclose a repeatable process to make the recited WC196Δrmf.

***Conclusion***

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

9. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CLF

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SUPERVISORY PATENT EXAMINER
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